DOCKET NO. 17710 (AP) PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Application of
Old et al.

Serial No: 10/564,829

Filed: January 13, 2006

For: 5-THIO-PIPERDINYL PROSTAGLANDIN E ANALOGS

Group Art Unit: 1609

Examiner: David E. Gallis

Confirmation No. 3665

DECLARATION OF AN EXPERT REGARDING FACTS RELEVANT TO PATENTABILITY (37 C.F.R. § 1.132)

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

PURPOSE OF DECLARATION

1. This declaration is to establish evidence of patentability of one or more claims of the above referenced application.

2. The persons making this declaration is an expert in the relevant art.

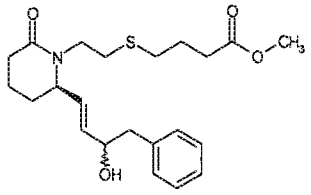
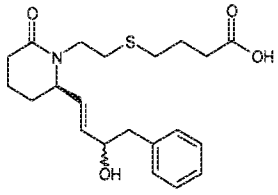
3. The person making this declaration is an employee of the Assignee, Allergan, Inc.

TESTIMONY OF EXPERT RELEVANT TO PATENTABILITY

4. The data in Table 1 below demonstrates that the compounds shown in the Table are prostaglandin EP4 agonists.

5. A person of ordinary skill in the pharmaceutical art can reasonably estimate a therapeutically effective dose of a compound by performing an assay such as those used to obtain the data obtained in Table 1, and by carrying out routine pharmacokinetic studies.

Table 1

Structure	Binding Data		Functional Data (EC50 in nM)							
	hEP2	hEP4	hFP	hEP1	hEP2	hEP3A	hEP4	hTP	hIP	hDP
		4477	NA	NA	NA	NA	81	NA	NA	NA
		52	NA	NA	NA	NA	0.92	2661	NA	NA

6. All data in Table 1 was obtained using routine procedures.

7. The functional data was obtained using the procedure described in U.S. Patent Application Serial No: 10/564,829, starting on p. 24, line 12 as "(b)

8. **CALCIUM SIGNAL STUDIES ON THE FLIPR™**."

9. The binding data was obtained by the following procedure. Competition binding experiments were performed in a medium containing Hank's balanced salt solution, Hepes 20 mM, pH 7.3, membranes (~60 µg protein) or $2x10^5$ cells from HEK 293 cells stably expressing human EP4 receptors, [^{3}H]PGE2 (5 nM) and various concentrations of test compounds in a total volume of 300 µl. Reaction mixtures were incubated at 23 °C for 60 min, and were filtered over Whatman GF/B filters under vacuum. Filters were washed three times with 5 ml ice-cold buffer containing 50 mM Tris/HCl (pH 7.3). Non-specific binding was estimated in the presence of excess unlabeled PGE2 (10 µM). Binding data fitted to the binding model for a single class of binding sites, using nonlinear regression analysis. IC_{50} values thus obtained were converted to Ki using the equation of $Ki=(IC_{50}/(1+[L]/K_D)$ where [L] represents PGE2 concentration (5 nM) and K_D the dissociation constant for [^{3}H]PGE2 at human EP4 receptors (4.3 nM).

TIME OF PRESENTATION OF THE DECLARATION

This declaration is submitted prior to final rejection.

DECLARATION

4. As a person signing below:

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on Information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

SIGNATURE(S)

7. Expert in the Pharmaceutical Art

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